IAPS Rec'd PCT/PTD 1

Approved for use through 3/31/2007. OMB 0651-0021 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number. ATTORNEY'S DOCKET NUMBER JHU2010-1 TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) U.S. APRAIGATION NO! (Iliknown, Gee 38 CFR 1.5) **CONCERNING A SUBMISSION UNDER 35 U.S.C. 371** INTERNATIONAL APPLICATION NO. PCT/US2004/022698 INTERNATIONAL FILING DATE PRIORITY DATE July 15, 2004 July 15, 2003 TITLE OF INVENTION ELEVATED HEDGEHOG PATHWAY ACTIVITY IN DIGESTIVE SYSTEM TUMORS, AND METHODS OF TREATING DIGESTIVE SYSTEM TUMORS HAVING ELEVATED HEDGEHOG PATHWAY ACTIVITY APPLICANT(S) FOR DO/EO/US Philip A. Beachy, David Monty Berman, Sunil S. Karhadkar and Anirban Maitra Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information: 1. A This is a FIRST submission of items concerning a submission under 35 U.S.C. 371. This is a SECOND or SUBSEQUENT submission of items concerning a submission under 35 U.S.C. 371. This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below. The US has been elected (Article 31). \boxtimes A copy of the International Application as filed (35 U.S.C. 371 (c)(2)) is attached hereto (required only if not communicated by the International Bureau). a. has been communicated by the International Bureau. C. is not required, as the application was filed in the United States Receiving Office (RO/US). 6. An English language translation of the International Application as filed (35 U.S.C. is attached hereto. has been previously submitted under 35 U.S.C. 154(d)(4). 7. Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3)) are attached hereto (required only if not communicated by the International Bureau). a. ☐ have been communicated by the International Bureau. b. have not been made; however, the time limit for making such amendments has NOT expired. C. d. A have not been made and will not be made. 8. 🔲 An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)). 9. An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). (unsigned) 10. 🗌 An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)). Items 11 to 20 below concern document(s) or information 11. An Information Disclosure Statement under 37 CFR 1.97 and 1.98. 12. An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included. 13. A preliminary amendment. 14. An application Data Sheet under 37 CFR 1.76. 15. A substitute specification. 16. A power of attorney and/or change of address letter.

20. Other items or information: Certificate of Mailing under 37 CFR 1.10 (EV 841 622 602 US); Check No. 580473 in the amount of \$1,640.00; Recording of a Change; ISR/Written Opinion; Return Receipt Postcard.

17. A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821 - 1.825.

19. A second copy of the English language translation of the International Application under 35 U.S.C. 154(d)(4).

18. A second copy of the published International Application under 35 U.S.C. 154(d)(4).

This collection of information is required by 37 CFR 1.414 and 1.491-1.492. The information is required to obtain or retain a benefit by the public, which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 15 minutes to complete, including gathering information, preparing, and submitting the completed form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Mail Stop PCT, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

APPLICATION NO. (if known, see 37 CER. INTERNATIONAL APPLICATION NO. | ATTORNEY'S DOCKET NUMBER.

U.S. APPLICATION	ON NO. (if know	n, see 37 CFR	INTERNATIONAL A				OCKET NUMBER
20,004,000						JHU2010-1	
The following fees are submitted:						CALCULATIONS	PTO USE ONLY
21. ☒ Basic national fee						\$ \$300.00	
22. Examina If International pre satisfy provisions of All other situations	liminary examina of PCT Article 33	\$ \$200.00					
23. Search fee Search fee (37 CFR 1.445(a)(2)) has been paid on the international application to the USPTO as an International Searching Authority \$100 International Search Report prepared and provided to the Office \$400 All other situations \$500						\$ \$100.00	
TOTAL OF 21, 22 and 23 = Additional fee for specification and drawings filed in paper over 100 sheets (excluding						\$ \$600.00	
sequence listing or computer program listing filed in an electronic medium). The fee is \$250 for each additional 50 sheets of paper or fraction thereof.							
Total Sheets Extra Sheets		Number of each additional 50 or RATE fraction thereof (round up to a whole					
46 - 100 =	0 /50 =	<u> </u>	0	×	\$250.00	\$ \$0.00	
Surcharge of \$130 months from the e	arliest claimed p	\$ \$130.00					
CLAIMS	NUMBER	FILED	IUMBER EXTRA	R	ATE		
Total claims	67	- 20 =	47	х	\$50.00	\$ \$2,350.00	
Independent claim	s 4	- 3 =	11	х	\$200.00	\$ \$200.00	
Multiple Depend	ent Claims (if a			+	\$360.00	\$	
TOTAL OF ABOVE CALCULATIONS = Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are						\$ \$3,280.00	
reduced by 1/2.						\$ \$1,640.00	
SUBTOTAL =						\$ \$1,640.00	
Processing fee of \$130.00 for furnishing the English translation later than 30 months from the earliest claimed priority date (37 CFR 1.492(i)).						\$	
TOTAL NATIONAL FEE =						\$ \$1,640.00	
Feè for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per +						\$	
TOTAL FEES ENCLOSED =						\$ \$1,640.00	
						Amount to be refunded:	\$
						Amount to be charged:	\$
a. 🛛 A check in the amount of\$1,640.00 to cover the above fees is enclosed.							
b. Please charge my Deposit Account in the amount of to cover the above fees. A duplicate copy of this sheet is enclosed.							
c. The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account 07-1896 . A duplicate copy of this sheet is enclosed.							
d. Fees are to be charged to a credit card. WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.							
NOTE: Where an appropriate time limit under 37 CFR 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the International Application to pending status.							
SEND ALL CORRESPONDENCE TO:							
Lisa A. Haile, J.1	D., Ph.D.	KIO	,·0.				
DLA Piper Rudnick Gray Cary US LLP 4365 Executive Drive, Suite 1100 SIGNATURE						- Va	<u>ce</u>
4365 Executive I San Diego, CA 9	•	•					
						isa A. Haile, J.D., Ph.D.	
NAME							
January 13, 2006 REGISTRA						38,347 TION NUMBER	

IAP6 Rec'd PCT/PTO 13 JAN 2006

PATENT

ATTORNEY DOCKET NO.: JHU2010-1

Certificate of Mailing under 37 CFR § 1.10

"EXPRESS MAIL" Mailing Label Number: EV 841 622 602 US
Date of Deposit: January 13, 2006

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Enclosures:

- 1. Form PTO-1390 (2 pgs in duplicate);
- 2. Preliminary Amendment (3 pgs);
- 3. Declaration (unsigned) (4 pgs);
- 4. Certificate of Mailing under 37 CFR § 1.10 (1 pg);
- 5. Notification of Transmittal of the International Search Report and the Written Opinion of the International Searching Authority, or the Declaration (12 pgs);
- 6. Notification of the Recording of a Change (1 pg);
- 7. Check No. 580473 in the amount of \$1,640.00; and
- 8. Return Receipt Postcard.

Karen LePari

Name of Person Mailing Papers

Karen De Pau,